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(71) Applicant (for all designated States except US): **MERCK & CO., INC.** [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065-0907 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **DOHERTY, George, A.** [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065-0907 (US). **HALE, Jeffrey, J.** [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065-0907 (US).

(74) Common Representative: **MERCK & CO, INC.**; 126 East Lincoln Avenue, Rahway, NJ 07065-0907 (US).

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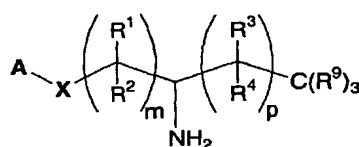
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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: AMINOALKYLPHOSPHONATES AND RELATED COMPOUNDS AS EDG RECEPTOR AGONISTS



(57) Abstract: The present invention encompasses compounds of formula (II); as well as the pharmaceutically acceptable salts and hydrates thereof. The compounds are useful for treating immune mediated diseases and conditions, such as bone marrow, organ and tissue transplant rejection. Pharmaceutical compositions and methods of use are included.

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/07262

## A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : A61K 9/127

US CL : 424/450

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)  
U.S. : 424/450

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched  
NONE

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)  
APS, CAS ONLINE

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	ISOGAI et al. Structures of Beta-Amino Acids in Antibiotics Iturin A. Tetrahedron Lett. 1982, Vol. 23, No. 30, pages 3065-3068.	1-6, 20
X	ENDER et al. Enantioselective synthesis of .beta. -amino acids: TMS-SAMP as a chiral ammonia equivalent for the aza analogous Michael addition to .alpha., .beta.-unsaturated esters. Angewandte Chemie International Edition in English. 1995, Vol. 34, No. 4, pages 455-457.	1-6, 20
X	NAKASHIMA et al. Pollen germination inhibition by .alpha.- and .beta. -aminoalkanoic acids. Chemistry Express, 1982, Vol. 7, No. 6, pages 481-484.	1-6, 20
X	PEYPOUX et al. Isolation of 3-amino-12-methyltetradecanoic acid and 3-amino-12-methyltridecanoic acid from iturin, an antibiotic of Bacillus subtilis. Tetrahedron. 1973, Vol. 29, No. 21, pages 3455-3459.	1-6, 20

☐ Further documents are listed in the continuation of Box C.

☐ See patent family annex.

* Special categories of cited documents:	
"A" document defining the general state of the art which is not considered to be of particular relevance	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"E" earlier application or patent published on or after the international filing date	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"O" document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family
"P" document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

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Mail Stop PCT, Attn: ISA/US  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, Virginia 22313-1450

Facsimile No. (703)305-3230

Authorized officer

Dave T Nguyen

Telephone No. 703-308-0196

DAVE T. NGUYEN  
PRIMARY EXAMINER

*Robert Collins*

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/07262

## Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claim Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claim Nos.:  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claim Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:  
Please See Continuation Sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1-6, 7, 8, 13, and 20, drawn to Species No. 1

Remark on Protest

☐  
☐

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

## INTERNATIONAL SEARCH REPORT

PCT/US03/07262

### BOX II. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claims 1-6, 7, 8, 13, 20, drawn to a composition comprising a compound represented by Formula II, the first identified method of using the composition to treat systemic lupus erythematosus.

Group II, claims 7-11, drawn to a method of using the composition to treat multiple sclerosis.

Group III, claims 7-10, 12, drawn to a method of using the composition to treat rheumatoid arthritis.

Group IV, claims 7-10, 14, drawn to a method of using the composition to treat psoriasis.

Group V, claims 7-10, 15, 19, drawn to a method of using the composition to treat a rejection of transplanted organ or tissue.

Group VI, claims 7-10, 16, drawn to a method of using the composition to treat an inflammatory bowel disease.

Group VII, claims 7-10, 17, drawn to a method of using the composition to treat a malignancy of lymphoid origin.

Group VIII, claims 7-10, 18, drawn to a method of using the composition to treat chronic lymphocytic leukemias and lymphomas.

Group IX, claims 7-8, 10, drawn to a method of using the composition to treat type I diabetes mellitus.

Group X, claims 7-8, 10, drawn to a method of using the composition to treat biliary cirrhosis.

Group XI, claims 7-8, 10, drawn to a method of using the composition to treat uveitis.

Group XII, claims 7-8, 10, drawn to a method of using the composition to treat Crohn's disease.

Group XIII, claims 7-8, 10, drawn to a method of using the composition to treat ulcerative colitis.

Group XIV, claims 7-8, 10, drawn to a method of using the composition to treat sarcoidosis.

Group XV, claims 7-8, 10, drawn to a method of using the composition to treat Autoimmune myositis.

Group XVI, claims 7-8, 10, drawn to a method of using the composition to treat Wegener's granulomatosis.

Group XVII, claims 7-8, 10, drawn to a method of using the composition to treat Ichthyosis.

Group XVIII, claims 7-8, 10, drawn to a method of using the composition to treat Graves ophthalmopathy.

Group XIX, claims 7-8, 10, drawn to a method of using the composition to treat Asthma.

This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

## INTERNATIONAL SEARCH REPORT

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In order for more than one species to be examined, the appropriate additional examination fees must be paid. The species are as follows:

Claims 1-20 embrace an enormous number of compounds, wherein each of the compounds is drawn to a particular combination of identifiers, wherein each of the identifiers corresponds to a particular molecule as listed in the claims.

Note that the following species (identified as species No. 1) will only be searched should applicant does not pay for additional examination fees:

Species No. 1: A compound represented by Formula II as set forth in claim 1, wherein  $m = 1$ ,  $p = 9$ , X is a bond, A is  $-CO_2H$ , each  $R^1$  is a hydrogen, each  $R^3$  is a hydrogen,  $R^2$  and  $R^4$  is a hydrogen, R8 is a  $C_{1-4}$  alkyl group,  $R^9$  is a hydrogen.

Otherwise, each of the additional species, which are at least 20, wherein m, p, X is a bond, A, each  $R^1$ , each  $R^3$ ,  $R^2$  and  $R^4$ , R8,  $R^9$  must be clearly identified for a particularly named chemical compound, will only be searched if an appropriate additional fee is paid.

The claims are deemed to correspond to the species listed above in the following manner:

Claims 1-20, which embrace an enormous number of compounds (at least 20) as indicated above.

The following claim(s) are generic: Claim 1.

The inventions listed as Groups I-XIX do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

Each of the Group I-XIX is directed to a distinct method of treatment for a disease having a distinct symptom and functional effect. For example, the treatment of Crohn's disease is completely distinct from a treatment of asthma, let alone all other diseases listed in the laundry list cited in claim 10. Each of the methods is expected to generate a distinct functional effect. Furthermore, 37 CFR 1.475 does not provide for multiple independent products, methods of manufacture and methods of use (37 CFT 1.473(d)).

The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons: each of the particular combination of compounds corresponding to each identifier so as to make up the entire molecule of formula II is a distinct compound having a distinct function and effect in a treatment of an immunoregulatory abnormality. Given the variability among the identifiers and/or combinations thereof as employed in Formula II, Formula II, which clearly embrace distinct compounds, does not constitute a substantially common structure with a single general inventive concept.